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# Spatiotemporal characteristics of hemodynamic changes in the human lateral prefrontal cortex during working memory tasks

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**Subject: Memory and Emotion**

**Abstract**

[INTRODUCTION]

Although most agree that the lateral prefrontal cortex (PFC) plays a critical role in working memory (WM), the localizations of its central executive (CE) and two slave systems are still subject to debate. Both the executive control and active maintenance of stored information are necessary for proper WM performance. It is supposed that regional brain activation attributed to the executive control is sustained throughout the task, while that related to the active maintenance may vary with time. Therefore, it is expected that dynamic recording of changes in regional cerebral flow (rCBF) associated with the lateral PFC can help improve our understanding of the organization of WM. Using near-infrared spectroscopy (NIRS), we examined the spatiotemporal changes in oxy-Hb, an indicator of changes in rCBF, during two WM tasks having differing degrees of CE involvement.

[METHODS]

Twelve healthy, right-handed volunteers (11 males, 1 female, 21-29 years old) performed the n-back (n=0, 1, 2, 3) and the random number generation (RNG) tasks. The order of n-back and RNG tasks was randomized. All tasks were repeated twice in a counterbalanced fashion. Continuous NIRS recording was made with a 20-channel NIRS system (OMM-2000, Shimadzu). Seven of the 12 subjects underwent MRI in order to determine the exact anatomical positions of the eight incident-and-detecting light-guide pairs. After each session, quantitative optical pathlength between each light-guide pair was obtained using a 1-channel time-resolved spectroscope (TRS-10, Hamamatsu K.K). The optical topographical activation was reconstructed by first subtracting the control oxy-Hb image from the test before superimposing on the 3-D MRI image. The temporal profiles of oxy-Hb changes within each activated area were then examined.

[RESULTS]

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Activation from the ventrolateral prefrontal cortex (VLPFC) was prominent with both n-back and RNG tasks. There was sustained as well as non-sustained activation. Non-sustained activation means the oxy-Hb first increases but then decreases to or below the baseline level before the end of the task. For the n-back task, 8 of the 12 subjects showed a positive correlation between the VLPFC activation and the number of elements stored in WM. Most activation was bilateral. For the RNG task, there was more dorsolateral prefrontal cortex (DLPFC) activation as compared to the n-back task. The activation was largely sustained and more right-hemisphere-dominant. When the same lateral PFC from both hemispheres was activated, synchronous changes in oxy-Hb were observed.

[CONCLUSION]
The VLPFC and DLPFC in both hemispheres were probably responsible for active maintenance common in both of the WM tasks. It is plausible that there is additional CE involvement with the RNG than with the n-back task. Therefore, it is supposed that the increased sustained DLPFC activation observed on the right hemisphere with the RNG task reflects this extra control.

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## AIMS

Although most agree that the prefrontal cortex (PFC) subserves several cognitive processes such as manipulation and monitoring that are ascribed to the central executive (CE) of working memory (WM), the CE remains to be specified and its localization is still subject to debate. This study was aimed to elucidate an entity of the CE.

If the CE can be isolated from other cognitive processes in WM and is discretely localized, it is postulated that there is regional brain activation, which is sustained throughout the task, in common with all the WM tasks.

It is expected that dynamic recording of changes in regional cerebral flow (rCBF) associated with multiple regions of the lateral PFC can help improve our understanding of the functional organization of the PFC with respect to the CE.

Using near-infrared spectroscopy, thus, we examined temporal characteristics of changes in oxygenated hemoglobin (oxy-Hb), an indicator of changes in regional cerebral blood flow (rCBF) in both sides of the lateral PFCs during two WM tasks (n-back and random number generation (RNG) tasks).

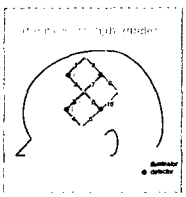
## METHODS

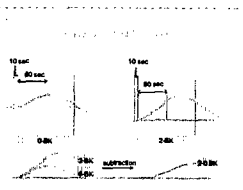
12 healthy right-handed paid volunteers (age range, 21-29, male 11, female 1).

24-channel NIRS imaging system
(OMM 2000, Shimadzu Co.)
1-channel time-resolved spectroscopy (TRS-10, Hamamatsu Photonics KK.)

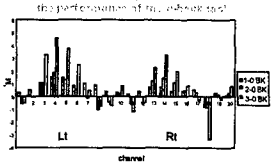
Participants viewed a sequence of random digits on a computer display. The digits were limited to the values 1, 2, 3, and 4. The inter-digit interval was 1.8 seconds. Prior to a digit series, participants were instructed to remember the "target" digit that was n-back (0, 1, 2, or 3 digits back in the sequence). Using their left hand, participants responded by pressing the key that corresponded to the target digit.

Participants were asked to recite a sequence of random numbers between 0 and 9. As the control, they were asked to repeatedly count out loud in order from 0 to 9 to a 1 Hz pacing tone.






(1)Sum of increases in oxy-Hb in each side was calculated.
(2) When this value in the one side (Left or Right) is less than 70 % of that in the other side, it was considered that the hemispheric laterality existed.



## RESULTS

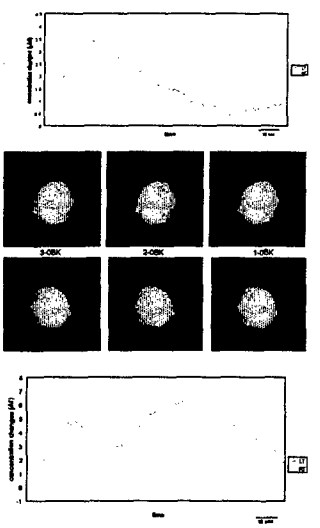
1. Mean correctness for the 2- and 3-back tasks were 93% (SD = 8%) and 83% (SD = 24%), respectively. Five of 12 participants performed poorly in the RNG task showing either counter or interval bias (Table 2).
2. Activation from the ventrolateral prefrontal cortex (VLPFC) was prominent with both n-back and RNG tasks (Table1). These VLPFC activation was sustained as well as non-sustained. Non-sustained activation means that the oxy-Hb first increases but then decreases to or below the baseline level before the end of the task (Fig. 1).
3. For the n-back task, 8 of the 12 participants showed a positive correlation between the VLPFC activation and the number of elements stored in WM (Fig. 2).
4. For the RNG task, the activation was more right-hemisphere-dominant (Table 1). Also, as compared to the n-back task, activation was largely sustained (Table 2).
5. It should be noted that when the same lateral PFC from both hemispheres was activated, synchronous changes in oxy-Hb were observed (Fig. 3).

| subjects | 3-0 BK | | | R-S | | |
|---|---|---|---|---|---|---|
| | LT | RT | laterality | LT | RT | laterality |
| 1 | V | V | L | V | V | L |
| 2 | D | V | | D | D | |
| 3 | V | V | | - | BA8 | |
| 4 | V | V | | D | D/BA8 | |
| 5 | D, BA8 | V | L | V | V | |
| 6 | V | V | | V | V | |
| 7 | V | V | | V | V | |
| 8 | V | V | | D | V | |
| 9 | D/BA8/V | BA8/8 | L | D/BA8 | - | L |
| 10 | V | V | | V | V | |
| 11 | V | V | | V | V | |
| 12 | V | D | | D | D/BA8 | L |

V; VLPFC, D; DLPFC, BA; Brodmann's area, L; left, R; right, B; bilateral

| subjects | 3-0 Bk | | | R-S | | |
|---|---|---|---|---|---|---|
| | LT | RT | task performance (%) | LT | RT | task performance |
| 1 | | | 86.5 | V→ | V→ | -CB |
| 2 | D→ | | 93.5 | D→ | D→ | CB, -CB, IB |
| 3 | | | 97.5 | — | BA8→ | RB, -CB |
| 4 | V→ | V→ | 88 | D→ | D/BA8→ | -CB |
| 5 | | | 95 | | | |
| 6 | | | 80.5 | | | |
| 7 | V→ | V→ | 62.5 | V→ | V→ | |
| 8 | | V→ | 96 | D→ | D→ | |
| 9 | D/BA8/V→ | BA8/8→ | 80.5 | D/BA8→ | — | |
| 10 | | | 88 | V→ | V→ | |
| 11 | | | 14 | V→ | V→ | CB |
| 12 | V→ | D→ | 99 | D — | D/BA8→ | |

↓; decrease to the baseline, (↓); decrease without reaching the baseline, →; increase with or without a plateau, CB; counting bias, IB; interval bias, RB; repetition bias

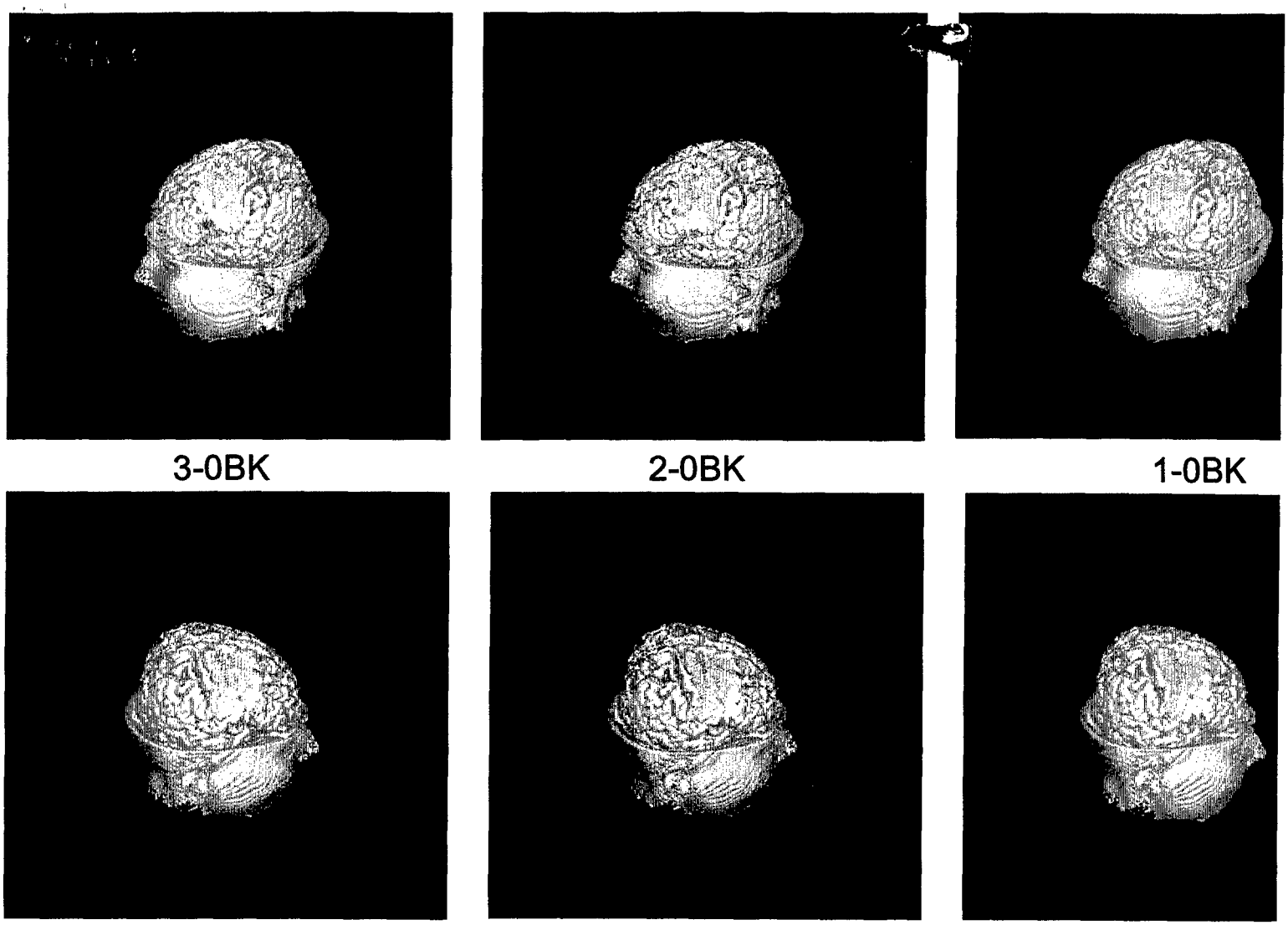



## CONCLUSIONS

These data suggest that at least within the lateral PFC measured in this study, the CE is not represented in a unified system, but it stems from neural pathways needed for task performance.

Non-sustained increases in oxy-Hb may be explained by uncoupling between neuronal activity and CBF.

Bilateral increases in CBF do not necessarily mean the bilateral activation. It is plausible that the strong activation on the one side is transmitted to the other side through the neural connections between the hemispheres.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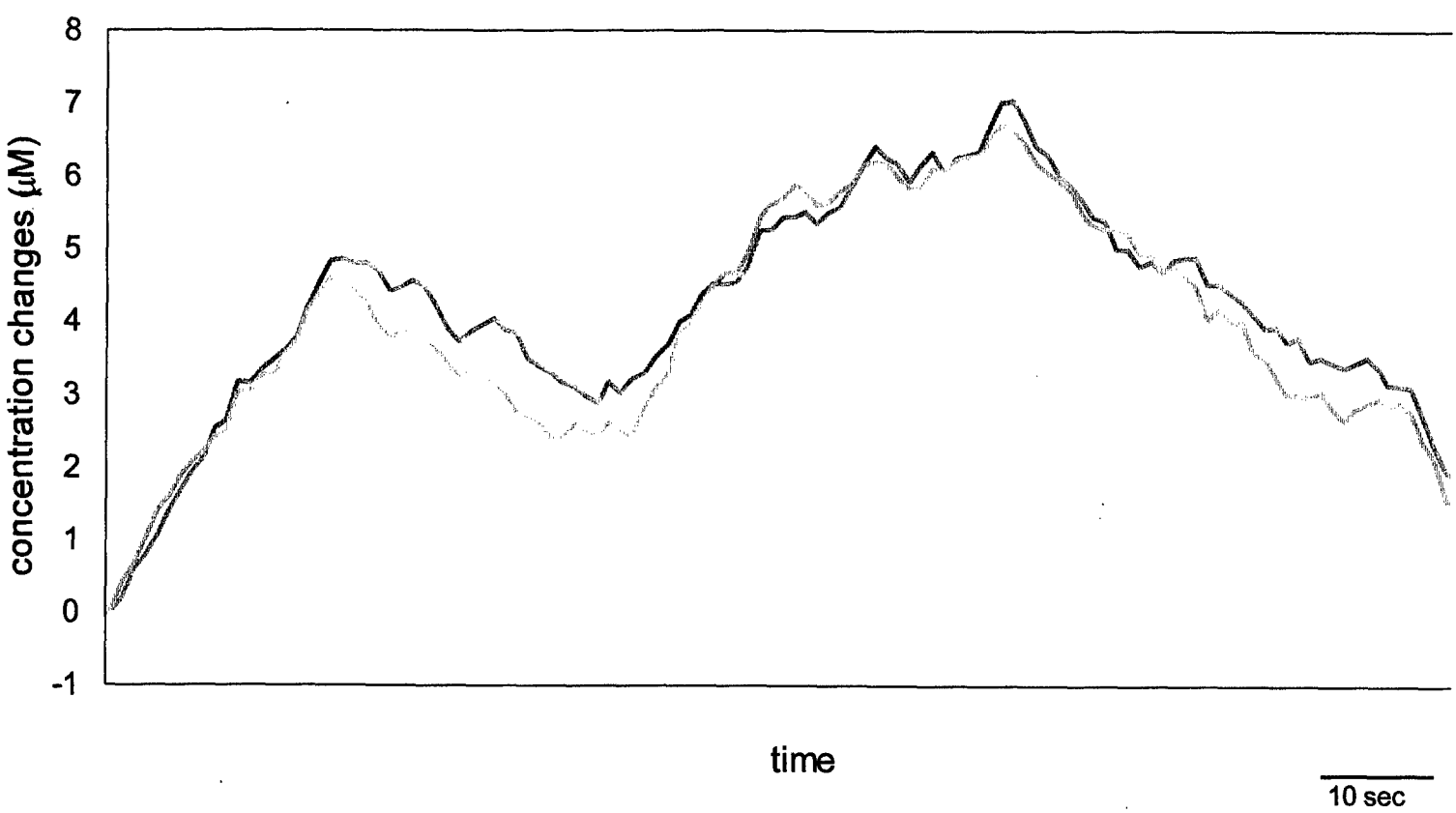
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concentration changes (μM)
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